Indian Journal of Psychology and Education
January, 2025, Vol. 15 No.1, pp 52-57

# Transcranial Direct Current Stimulation: Contemporary Intervention Techhnique in Treatment of Mental Illnesses: A Review

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**Abstract**

Mental Illnesses (MI) is characterized by disruption of cognitive functioning, emotional regulation, and behavioural pattern in an individual. These symptoms causes substantial distress and impairment in key areas of functioning. MI affects millions globally and it significantly impacts their quality of life, and many among those who seek treatment do not achieve remission with current treatments and standard interventions. Therefore, there is a critical need for novel and effective approaches to improve outcomes in the management of MI. A contemporary technique in the field of MI treatment is the application of Transcranial Direct Current Stimulation (tDCS). Recent research has indicated that tDCS can be a promising non-invasive brain stimulation technique in psychiatry, with applications in major depressive disorder, schizophrenia, obsessive-compulsive disorder, substance use disorders and as a promising avenue for cognitive enhancement. We will discuss the current knowledge regarding the efficacy, safety, and potential mechanisms of action of tDCS in the treatment of MI which might help pave way for the development of personalized and targeted interventions to improve outcomes for individuals with MI.

**Key-words:** Transcranial direct current stimulation, Contemporary Technique, Neuromodulation, Mental Illnesses, Cognition, Review.

The idea of electrical brain stimulation dates back to the Roman Empire, with Largus, S. (1529) describing the use of electric jolt from "torpedo fish" to treat headaches. In 1802, Aldini G. reported the first cortical stimulation using a voltaic pile for transcranial electrical stimulation to treat depression then referred to as melancholia. The development of the voltaic battery paved the way for the application of electrotherapy in the medical field, with physicians using galvanic batteries for electric brain stimulation in the 19th and 20th centuries. However, these early interventions were largely uncontrolled. Systematic research began in the 1950s and 1960s, exploring the therapeutic potential of feeble direct current (DC) stimulation on cortical excitability in animal and human subjects with depression or mania. Research on tDCS waned in the mid-20th century due to the negative perception surrounding electroconvulsive therapy (ECT) and the rise of psychopharmacological treatments. However, Kuo, M. F., & Nitsche, M. A. (2012) findings demonstrating tDCS's ability to induce lasting neural changes in healthy subjects has reignited research interest in this technique over the past two decades. tDCS holds promise as a potential treatment for a wide array of psychiatric disorders and neurological conditions, including major depressive disorder, anxiety disorders, obsessive compulsive disorder and schizophrenia etc.

**tDCS: Technical Aspects and Mechanism of Action**

tDCS is a non-invasive brain stimulation technique utilizing low-intensity, direct current delivered to the scalp via electrodes. Its operation is governed by Ohm's Law, relating voltage, current, and resistance. A tDCS device delivers a constant, predefined electric current through two electrodes on the head, with the current passing between them determined by the electric potential difference and resistance. tDCS induces sub threshold modulation of neuronal excitability, shifting membrane voltage by less than 1 mV. This effect is considered subthreshold, as it doesn't directly trigger action potentials but instead alters neural network dynamics. This significantly stimulates superficial cortical areas, modulating neuronal excitability without triggering action potentials as reported by Bikson, M et al, 2004. The polarity of the electrodes determines the effect: stimulation at anode excites cortical region to which it is applied, while region with cathode stimulation decreases excitation. Resulting effects can last up to 2 hours post stimulation. The effects of tDCS are determined by electrode polarity, dose (current intensity: 0.5-2 mA, duration: 5-40 min, electrode size: 3-100 $cm^2$), and current density, Zaghi et al 2010. Electrode placement is typically guided by the international EEG 10-20 System, DaSilva et al 2011. The flow of electric current originates at the anode, passing through the scalp, skull and cortical regions, before it finally exits at the cathode following shortest path.

**t-DCS and safety concerns**

tDCS is considered a safe technique with mild, transient and reversible adverse effects. A meta-analysis by Brunoni et al. 2011 found that the most common adverse effects in the active group were reversible and included mild itch sensation, tingling, pricking sensation, and mild discomfort that resolves on its own immediately or few minutes after the device is removed. tDCS has been found to have a reasonably safe profile, with limited side effects, when applied within conventional parameters (≤40 min, ≤4 mA).

**Use of t-DCS in treating Mental Ilnesses**

As a brainstimulation tool, tDCS was reconsidered again in current century. In a seminal study Priori et al. (1998) demonstrated that application of weak, direct current via scalp electrodes induce lasting

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changes in cortical excitability, demonstrating that anodal stimulation enhances while cathodal stimulation suppresses neuronal activity. The precise mechanisms of action of tDCS remain an area of active research. Current understanding suggests that tDCS exerts its effects by inducing subtle changes in membrane potential, lesser than 1 millivolt. These minute changes are hypothesized to modulate neuronal firing patterns and consequently influence the overall level of cortical excitability Datta et al., 2009. Other neuromodulation techniques like rTMS (repetitive transcranial magnetic stimulation), are expensive, requires sophisticated equipments and involves complex mechanisms as compared to tDCS which is inexpensive, has ease of use and can be carried anywhere easily. These characteristics are lucrative and hence researchers are increasingly interested in exploring tDCS as a contemprorary technique in treatment if Mental Illnesses. So far increasing evidence of positive results in major depression and schizophrenia is on the rise.

**Use of t-DCS in treatment of Major Depressive Disorder (MDD)**

MDD is a severe, chronic, and prevalent psychiatric disorder, with a life prevalence of 6-12% and a yearly prevalence of 3-11% worldwide, Kessler et.al. 2010. Out of those who receive treatment, 80% of patients experience relapse of depressive symptoms, and approximately 33% do not reach complete remission, Nemeroff, C.B. 2007. Neuroimaging studies indicate impaired neural circuits connecting brain regions that are responsible for emotional regulation, primarily prefrontal cortex and limbic system in MDD. More recent models suggest that MDD may be caused from imbalances of neural networks responsible for processing emotions and cognitive control (Hamilton et al., 2011). Imbalanced activity between these systems can lead to attention impairment, negative emotion identification, and cognitive deficits in MDD, Price J. L., & Drevets, W. C. (2010). The use of tDCS in MDD is based on several rationales, including prefrontal asymmetry theory, improvement in working memory and affective processing, and top-down neuromodulatory effects. Woodham et al 2024 in their randomized sham-controlled trial have found depressive symptoms showed significant improvement with tDCs usage. However, a study by Loo et al. 2010 found negative results. The largest controlled study to date, conducted by Brunoni et al.2013, found significant improvement in depressive symptoms with active tDCS, either seldom or coupled with sertraline. Randomized controlled trials (RCTs) initially supported the use of transcranial direct current stimulation (tDCS) targeting the dorsolateral prefrontal cortex for treating depression.However, more research is needed in this regard to establish an effective protocol to be used in MDD.

**Use of t-DCS in treatment of Bipolar Disorder**

Bipolar Disorder is a Mental Illness characterized by episodes of intense emotional states affecting a person's mood shifts, levels of energy and can hinder the ability to function. Bipolar disorder has a significant genetic component, with a 9% risk in first-degree relatives and 40-50% concordance in homozygous twins, Schotte et al 2006. Neuroimaging studies Newberg et al 2008 have indicated that regions of pre frontal cortex and amygdala were involved in emotional regulation and non invasive tDCS can be a tool to stimulate these regions. Brunoni et al 2011 included 31 subjects suffering from depression (Bipolar depression 14 + Unipolar depression 17) found that anodic tDCS over the left DLPFC reduced depressive symptoms in both groups, with effects lasting up to a month. Another study by Loo et al 2012 found limited results in the RCT phase but more promising outcomes in follow-up. Further studies are needed to validate tDCS as a treatment for bipolar depression.

**Use of t-DCS in treatment of Schizophrenia**

Schizophrenia is a mental illness which affects 0.5%-1.5% of the population, it is characterized by positive, negative, and cognitive symptoms, McGrath et al 2008. A study by Leucht et al. 2013 reported upto 40% of patients do not respond to treatment as expected suggesting that traditional antipsychotics have limited efficacy. Recent meta-analyses suggest promising results with repetitive transcranial magnetic stimulation (rTMS) for auditory verbal hallucinations and negative symptoms Shi et al 2014. Neuroimaging studies have linked these symptoms to abnormal brain activities in fronto-temporal and prefrontal cortex regions Jardri et al 2011. tDCS has been considered as a treatment for schizophrenia, with anode placed at left prefrontal cortex and cathode placed at left temporo-parietal junction Mondino et al 2014 reported hypothesized reduction of positive symptoms. Bifrontal tDCS has also been investigated for negative symptoms. Studies have reported promising results, with significant improvement in negative symptoms Bunse, T 2014 and case studies highlighting potential interest in reducing resistant negative and catatonic symptoms Narayanaswamy et al 2014. Agarwal et al 2013 & Poreisz et al 2007 showed tDCS seem to be safe in the brief periods, with mild reversible unwanted effects such as tingling, itching sensation. Further research is needed to confirm these findings and establish optimal stimulation parameters.

**Use of t-DCS in Obsessive Compulsive Disorder (OCD)**

Obsessive-compulsive disorder (OCD) is a MI. Fontenelle et al 2010 found there is 2% prevalence across lifetime, causing severe impairments in functioning. Foa et al 2005 found pharmacotherapy and cognitive-behavior therapy (CBT) are effective in only 40%-60% of patients, and 30% are unresponsive to treatment. OCD is believed to arise from disruptions within the cortico-striato-thalamo-cortical (CSTC) circuitry, encompassing key brain regions such as the prefrontal cortex and basal ganglia, Milad

et al., 2012. D'Urso et al 2014 in their study explored tDCS as a treatment for OCD, with cathode placement to the pre-supplementary motor area (pre-SMA) reduced symptoms. The pre-SMA is thought to be hyperactive in OCD patients, and inhibitory tDCS may help normalize this activity. Electric flow models suggest that cathodal tDCS to the pre-SMA, with an extracephalic anode, may effectively target OCD-related brain areas Senco et al 2014.

**Use of t-DCS in Childhood & adolescent mental disorders**

Mental disorders often have an onset in childhood or adolescence, and there is need for early intervention too. Studies have shown tDCS may offer a promising therapeutic tool, leveraging the brain's greater plasticity during development, Rubio et al 2011. However, studies concerning child and adolescent psychiatry are very scarce in this regard, and mostly limited. Preliminary findings suggest anodal tDCS may improve language acquisition in patients with autism spectrum disorder Schneider et al 2011 and is well-tolerated in youths with schizophrenia Mattai et al, 2011. Research on attention deficit hyperactivity disorder (ADHD) is still in its early phase, with anodal tDCS showing potential for enhancing cognitive performance, Castellanos et al 2012. However limited research appears of application of tDCS in developing brains, it's essential to consider the benefits and risks and tDCS should be used in developmental age only after convincing evidence is collected in adult populations.

**Use of t-DCS in substance use disorders**

Substance use disorders pose significant treatment challenges due to their impact on the brain's reward system, particularly the dopaminergic pathways and prefrontal cortex (Koob et al., 2013). tDCS has shown reliable results in treatment of these disorders involving stimulation of prefrontal cortex.

Studies have demonstrated:

- Cocaine: tDCS over the dorsolateral prefrontal cortex (DLPFC) reduced risky behaviors in cocaine-dependent users Gorini et al 2014
- Alcohol: bilateral tDCS over the DLPFC reduced craving and relapse probability in severe alcoholic subjects Klauss et al. 2014
- Nicotine: tDCS over the DLPFC reduced craving and cigarette consumption in smokers Fecteau et al. 2014
- Cannabis: tDCS reduced craving for marijuana in patients with cannabis dependence Boggio et al. 2010
- Various research suggests that tDCS may prove to be a contemporary technique for treating substance use disorders, but further research is needed to confirm its efficacy in this regard.

**t-DCS use in cognition**

tDCS studies Demirtas et al 2013 has shown promise in improving cognitive function in various psychiatric and neurological conditions, including major depressive disorder, Tortella et al 2014, schizophrenia, substance use disorders, and Alzheimer's disease Boggio, P. S 2012 Studies have demonstrated improvements in working memory, attention, executive functions, processing speed, and learning. In healthy subjects, tDCS has been found to enhance cognitive performance, including improved naming performance and reduced semantic interference Sela et al 2012. While these findings suggest tDCS as a potential tool for cognitive rehabilitation, the short-lived nature of the observed changes warrants further investigation to optimize its application in treatment of neurocognitive disorders.

**Regulatory issues and Ethical Concerns in use of t-DCS**

tDCS has reportedly low risk profile, is easy to administer, and inexpensive compared to other brain stimulation options. However, these characteristics increase the risk of misuse, highlighting the need for regulations based on protocol Cabrera et al 2014. Currently, tDCS devices are regulated for research purposes, requiring adherence to protocol. Clinical use requires regulation based on ethical concerns, safety, and empirical evidence. Despite increasing evidence of tDCS benefits, including a recent meta-analysis showing its effectiveness in treating acute depression Shiozawa et al 2014, no country has regulated its use. Regulation is often restrictive, influencing medical insurance coverage and public health policies. tDCS devices should be regulated as medical devices, and their use should be restricted to trained technicians under medical supervision. While there is still a need for advanced understanding of tDCS protocols and long-term use, it is being used as an off-label in some countries.

As tDCS becomes widespread, there is need of large scale, well designed clinical trials with well-defined parameters to quantify its correct clinical use to monitor short term and long-term effects, and cooperate with governmental regulation to safeguard patient autonomy and well-being, Hamilton et al. 2011.

**Conclusion**

This overview of tDCS in treatment of Mental Ilnesses highlights its potential as a contemporary treatment modality. Despite being a relatively recent area of research, tDCS has shown promising results in majority studies conducted so far. The growing interest in tDCS from academia, the public, and media underscores the need for rigorous scientific inquiry and ethical considerations. Transcranial direct current stimulation (tDCS) may improve depressive symptoms, but clinical trial outcomes are mixed, and further research is needed. Clinicians should inquire about tDCS use and document accordingly, given its increasing popularity. While future studies may demonstrate tDCS efficacy or harm, it's essential to recognize the limitations of current information and consider tDCS within the broader context of available treatments. To advance the field of tDCS, future research endeavors must prioritize robust study

designs with strong internal and external validity to facilitate the replication, expansion, and optimization of existing findings, while enabling a more thorough investigation of key parameters such as electrode size, stimulation intensity, session duration and number of sessions.

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